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CHEMICAL RESEARCH, DEVELOPMENT & ENGINEERING CENTER

CRDEC-TR-178

USE OF METHYL SALICYLATES AS A TRIALING CHEMICAL AGENT SIMULANT

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May 1990

U.S. ARMY ARMAMENT MUNITIONS CHEMICAL COMMAND

Aberdeen Proving Ground, Maryland 21010-5423

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	1990 May	Final, 88 Nov - 89 May

4. TITLE AND SUBTITLE
Use of Methyl Salicylate as a Trialing Chemical Agent Simulant

5. FUNDING NUMBERS
PR-665612

6. AUTHOR(S)
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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Cdr, CRDEC, ATTN: SMCCR-RSP, Aberdeen Proving Ground, MD 21010-5423

8. PERFORMING ORGANIZATION REPORT NUMBER
CRDEC-TR-178

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)
This report's objective was to provide a comprehensive assessment of the use of methyl salicylate (MS) as a trailing chemical agent simulant for operational testing (OT) for the U.S. Army Armor and Engineering Board. MS has been used for OT as a simulant for blistering agents in hard/threat analysis, collective protection, decontamination, and detection. It's used because it satisfies most of the selection criteria used to determine the suitability of any proposed chemical agent simulant. These criteria involve the medical/safety aspects, environmental impact, chemical/physical properties, sampling/detection/analytical methods, agent/simulant correlations, producibility, and transportation/storage/disposal requirements associated with a simulant. In evaluating MS against previously mentioned criteria, MS can be an acceptable OT trailing simulant for blistering agents in most test conditions. However, if spread behavior is of major interest for a given test, neat MS spreads differently than mustard on most surfaces (i.e., either chemical agent resistance coating or alkyd painted surfaces). The addition of thickener to neat MS may or may not help the given situation, depending on subsequent test characteristics of interest. If an odorless simulant is required, MS may not be suitable because it has the recognizable and distant odor of wintergreen.

14. SUBJECT TERMS
Methyl salicylate, Simulant selection criteria, Simulant use, Chemical agent simulants

15. NUMBER OF PAGES
61

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UL

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PREFACE

The work described in this report was authorized under Project No. 665712, Chemical Agent Moniter. This work was started in November 1988 and completed May 1989.

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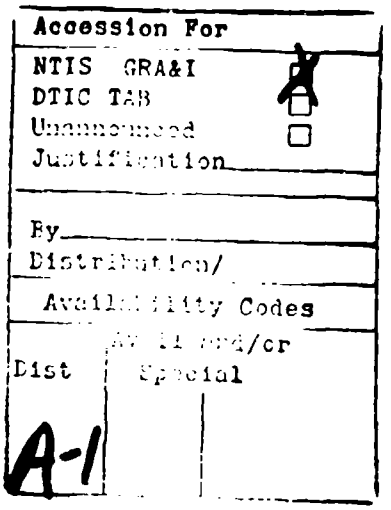

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USE OF METHYL SALICYLATE AS A TRIALING CHEMICAL AGENT SIMULANT

1. INTRODUCTION

1.1 Purpose.

This report provides a comprehensive assessment of the use of methyl salicylate (MS) as a trialing chemical agent simulant for operational testing (OT).

1.2 Background.

A simulant is a material which is substituted for a chemical agent due to either desired similar chemical or physical properties, or due to its ability to simulate chemical/physical reaction mechanisms of interest for an agent in a given environment. Simulants can be used for training or trialing purposes. Training refers to the process of learning to use equipment or to perform tasks. Trialing pertains to a scientifically designed and evaluated experiment for the research, development and testing of equipment which evaluates performance and utilization.

Methyl salicylate has been used as a chemical agent simulant for blistering (H) agents, such as mustard (HD), in both the laboratory and out in the field. Its usage is primarily due to similarities of some of its chemical/physical properties with mustard and its relative safety involving human exposure. Little[1] stated that MS, in relatively small quantities, has been approved by the Food and Drug Administration for its use in foods (50-3300 ppm) perfumes and anti-inflammatory ointments as a flavor/odor (oil of wintergreen) additive, and as a topical counterirritant, analgesic and/or anti-inflammatory agent. It was given generally recognized as safe (GRAS) status by the Flavor and Extract Manufacturers' Association in 1965.

2. METHYL SALICYLATE USAGE AS A TRIALING SIMULANT

Chemical agent simulants have been used to test the operation and performance of materiel for many years, but it has been only in the last 5-8 years that efforts to standardize the use of simulants have been initiated. In the past simulant use information obtained by an organization in the process of conducting a test was usually retained only by that organization. Now, databases are being formed containing simulant use information from the United States and other nations, and access to this information will aid in eliminating the obscure and unnecessary

research in testing with simulants. In general, the use of simulants to test materiel can be subdivided into seven categories:

a. Threat/Hazard - Simulation of dissemination mechanisms or the hazard created by a munition.

b. Individual Protection - Eye, skin, respiratory system and other body protection (i.e., mask, overgarments, boots).

c. Collective Protection - Exit/entry procedures and air purification design impacts for shelters and vehicles.

d. Decontamination - Simulation of the physical and chemical effects for decontamination equipment and solutions.

e. Materiel Protection - Equipment shipment containerization and cover design.

f. Medical - Prophylaxis and therapy.

g. Detection - Simulation of chemical warfare (CW) agent behavior in respect to warning, agent identification, contamination reconnaissance, and monitoring.

In an effort to prove out an item, more than just one of these simulant use categories is usually required, and to date no single chemical agent simulant has been developed to satisfy the requirements associated with each of the seven categories. Methyl salicylate is no exception, but compared with the other chemical agent simulants available it is one of the most used.

2.1 Threat/Hazard.

Methyl salicylate used at temperatures above -8.625 °C (its melting point) will be in liquid form. Test conditions are usually well above the melting point of MS, so its liquid form offers many mechanisms for it to be disseminated. U.S. Army Chemical Research, Development and Engineering Center (CRDEC), Human Use Protocol[2], utilized a hand-held garden sprayer to apply the simulant in a fine mist (droplet size 3 mm in diameter) to simulate the contamination likely to occur from a chemical agent bomb, missile, or other munition exploded or discharged in the air above a target area. Field tests with the Chemical Agent Monitor (CAM) have been conducted using 9- x 12- x 2-in. glass baking pans filled with MS as large vapor sources to simulate ground contamination. CAM performance testing also utilized 500 mL syringes with calibrated dispensers (Hamilton, Model PB 600) to contaminate small items and personnel with standard-size drops of a known concentration of MS. Vapor hazard studies have been performed with MS inside a M113 armored personnel carrier (APC) involving the desorption of MS vapor from contaminated patches of butyl rubber and overgarment material placed inside the vehicle. (Tytus, Cooper and Wasel[3]) A computer model predicting the vapor

concentration of MS within enclosures was also developed from the M113 APC research. (Tytus, Wasel and Cooper[4]) In addition to this computer model, other computer models have been developed to estimate the vapor hazard associated with indoor and outdoor spills (i.e., the D2PC Spill Model) of many chemicals including MS. Methyl salicylate can also be aerosolized, and studies are currently being conducted with MS investigating this latest threat.

2.2 Collective Protection.

Methyl salicylate has been used in exit/entry tests for both shelters and vehicles. (Blewett[5]; Blewett, Stickel, Arca, Hill[6]; Blewett, Stickel[7]; Blewett[8]) Specifically, using the previously referenced protocol, MS thickened with polymethylmethacrylate and mixed with a fluorescent tracer (Tinopal SWN) was applied to both vegetation and personnel in mission oriented protective posture (MOPP) IV gear. An area of vegetation was contaminated by the MS solution, and personnel travelled through in MOPP IV gear. The now contaminated personnel proceeded to enter the test shelter or vehicle according to the latest doctrine. An ultra-violet light was used to trace contamination brought into the shelter through subsequent contact (liquid transfer) by test personnel.

2.3 Decontamination.

Methyl salicylate has been used in studies (Long, Wallace[9]) investigating the effectiveness of various decontamination (decon) systems (i.e., hot air and hot water jet decon) in removing the simulant from various surfaces. Methyl salicylate was applied to a surface on a test substrate at a known uniform concentration. Decontamination of the test substrate was performed, and analysis of the test surface and/or the spent decon solution for MS determined how much MS remained on the test surface following decontamination. Test substrates were made from various steel and aluminum alloys and were painted or coated to investigate the effect the surface condition would have on the efficiency of decontaminating the surface. Some surfaces, for example, were coated with a polyurethane paint (CARC) and for comparison, other surfaces would be coated with an alkyd paint. Dirt or mud effects on a test surface have also been investigated. (Tytus, Wasel and Cooper[10])

2.4 Detection.

One of the most extensive areas of MS simulant usage was in the area of testing chemical agent detection equipment. The U.S. Army Armor and Engineering (AA&E) Board requested CRDEC support in designing their follow-on operational test and evaluation (FOT&E) for the CAM using MS as a simulant. The types of problems to be tested with the CAM are sorting contaminated personnel, and large/small equipment from clean personnel and

equipment (assuming a hasty decontamination situation); shelter contamination monitoring; f eld survey for key terrain, and field survey for limits of contamination (reconnaissance). The support role of CRDEC was to design contamination technology and monitoring methods to accomplish the goals of the FOT&E. These test goals were as follows:

a. CAM operational verification,
b. Test the man/machine interface,
c. Test the CAM use doctrine.

The test conditions and information gained allowed the AA&E Board to identify that test failure sources of error (equipment, man/machine interface, and doctrine) were random and ensured that simulant was present when required in the test matrix. It was also desired that a real-time record of contamination release be kept and that different levels of simulant "hazard" (concentration) be produced.

Investigation of the CAM's response to MS revealed that it was possible to produce predictable bar (hazard) response levels to the simulant for a given CAM, but not between CAMs. Also, real-time monitoring of MS using the MIRAN-1A infrared gas analyzer to support the CAM's bar readings would not be possible for all tests conducted. The lower limit of the MIRAN's ability to detect MS approaches the upper limit of the CAM before it becomes saturated. Due to this limitation, it was decided to use referee CAMs to backup the test CAM response of the soldier in the field. Another field test limitation taken into consideration was the control of MS concentration in space and time. It is likely that two CAMs samplings at slightly different times or locations will see very different concentrations due to shifts in the simulant vapor plumes even under relatively stable wind conditions. In addition to the CAM, M8 and M9 chemical agent detection papers respond to MS as they would to mustard.

3. SELECTION/USE CRITERIA FOR METHYL SALICYLATE

3.1 Medical/Safety.

The toxicity, dermal effects, and safety precautions associated ith MS and its exposure to personnel in using the simulant were investigated in this report and are evaluated in the following paragraphs.

3.1.1 Toxicity.

Methyl salicylate in small concentrations for use as a flavoring agent (50-3300 ppm) in food is safe, but it has been found that MS taken in small but concentrated amounts can be acutely toxic. A dose of 30 mL of concentrated MS (approximately

0.5 g/kg) may be fatal to adults, while a dose as small as 4-10 mL may be fatal to children or infants. (See Appendix A)

3.1.2 Dermal Effects.

Methyl salicylate is considered a strong dermal and mucous membrane irritant and can be absorbed through the skin. Precautions must be taken to avoid MS from being applied to the eyes or any mucous membrane due to the likelihood of severe irritation. Caution should also be exercised to avoid applying MS to already-irritated skin, wounds, and large areas of the body because of the toxicity of the MS that can be absorbed through the skin.

3.1.3 Safety Precautions.

While using MS as a trialing simulant, it is highly likely that test personnel will be both directly and indirectly exposed to chemical simulant. To minimize the amount of MS taken into the body by any route (i.e., oral, inhalation or skin absorption) the following precautions should be taken:

a. Wear protective/impermeable rubber gloves (i.e., M4 rubber gloves), a chemical apron and either chemical goggles or a face shield when handling liquid MS. The simulant will soften regular surgical gloves rendering them useless, so elbow-length protective rubber gloves (i.e., impermeable, M4, protective gloves conforming to MIL-G-12223G) offer the best protection from it being absorbed through the skin on your hands. Depending on the quantity of liquid simulant involved, a chemical protective gloves/apron/face shield or eye goggles combination should be worn when handling quantities of 10 mL or less, or a gloves/apron/face shield/shoe or boot covers combination for greater quantities should be worn to protect the eyes, face and rest of the body from simulant splatter from spills. Once liquid MS gets into leather or any regular clothing it is very difficult to remove even after multiple washing.

b. Wear a pressurized air hood, self-contained breathing apparatus, or a face mask (w/vapor filters) in conjunction with the suggested protective clothing when exposed to MS vapor concentrations greater than 600 mg/m^3.

c. Have some rags, kitty litter, or some other absorbent material readily available to soak up any MS accidentally spilled in handling.

The material safety data sheet (MSDS) for MS contains more specific information concerning precautions and other important MS safety data (i.e., chemical/physical properties, transportation, storage and hazard information).(See Appendix B)

3.2 Environmental Impact.

The U.S. Department of Transportation (DOT) does not list MS as a hazardous substance and MS is not listed as a hazardous waste according to the Resource Conservation and Recovery Act (RCRA). The environmental fate data (See Appendix C) on MS contains detailed information on its behavior in soil, water, and air when MS is released into the environment. When released in soil it will probably hydrolyze with moisture in the soil or biodegrade, and its reaction products eventually leach into the water table. Due to its low vapor pressure, very little MS will evaporate (volatilize) from the contaminated soil. If released in water it will probably hydrolyze at alkaline pH and biodegrade, but it will neither evaporate readily nor adsorb appreciably into sediments. It is also not likely that MS will bioconcentrate in aquatic organisms. Unfortunately, no atmospheric fate data has been reported for MS, but it was expected that MS would be oxidized by hydroxyl radicals with an estimated half-life of 5.7 days.

3.3 Chemical/Physical Properties.

See Appendixes B and C.

3.4 Sampling/Detection/Analytical Methods.

There are many methodologies for monitoring, sampling, and detecting MS as a vapor and liquid. The vapor can be detected with the MIRAN 1A, a 20 m optical path length infrared detector (minimum detectable limit approximately 1 ppm or 6.25 mg/m^3). Another method of analysis is the collection of MS vapor in sorbent tubes (filled with a given sorbent material), followed by thermal desorption into a gas chromatograph (GC) with a flame ionization detector (FID) or photoionization detector (PID). For example desorption tubes, filled with tenax having undergone a thermal desorption at 250 °C for 20 min, have yielded MS vapor recovery efficiencies of 95% with a minimum detectable limit of 0.2 micrograms. Ion chromatography, colorimetry, and fluorometry have also been used in a study to analyze the amount of MS desorbed from various sorbent materials to assist in developing a chemical agent and simulant dosimeter. (Dillon, Rose, Davis[11]) Another passive sampling technique developed for MS uses patches of latex rubber as adsorptive samplers. The MS vapor sampling rate is controlled by its rate of diffusion into the rubber, and the resultant MS concentration is determined through back calculations using a diffusion equation from the total mass of MS adsorbed into the rubber patch. The mass of MS adsorbed into the rubber is determined by extracting the MS from the patch with a 0.5 normal sodium hydroxide solution and analyzing the results colorimetrically. This technique produced a minimum detectable limit of either 1 microgram or 0.1 mg/m^3 for a 10 min sampling

period with a 2 - in. diameter patch. The CAM has been used to detect MS vapor in the concentration range of 0.1748 - 4.39 mg/m³ for a 2-6 bar response for a given test CAM.

Liquid MS can be analyzed by extracting the simulant from the test surface using a suitable solvent, one in which MS is soluble, and then analyzing by either GC or a previously mentioned spectrophotometric method. For example, liquid MS has been sprayed on personnel in MOPP IV protective gear, and then they underwent a hasty decontamination (decon) procedure. The protective overgarment was then placed in an ultrasonic bath of hexane which extracted the residual MS remaining in the clothing item. Subsequent GC analysis yielded a minimum detectable level of 1 ppm for the residual liquid MS retained by the protective overgarment after hasty decon. MS has also been applied to other clothing materials and painted surfaces and then extracted with ethanol and analyzed spectroscopically at 308 nanometers.

3.5 Application/Dissemination Methods.

Fortunately, MS both neat and thickened will be in liquid form when used in most test conditions, so this creates flexibility in how the simulant can be applied and disseminated. It can be poured into most containers opened to the atmosphere, thus creating a vapor source. The more vapor sources, or the greater the surface area of simulant exposed to the air, the greater the concentration of MS vapor generated downwind. Increasing the temperature of the simulant contained in the vapor source (when possible) will also increase the downwind concentration of MS vapor to a certain degree, because the evaporation rate of MS increases with temperature. A downwind MS vapor concentration can be determined by using any one of the analytical/detection procedures previously described in paragraph 3.4 for vaporized MS (i.e., MIRAN 1A or CAM).

Liquid MS can be brushed on or sprayed directly to contaminate a given area or item of interest. The desired area of contamination, surface condition, simulant dissemination uniformity, and surface contamination concentration are all important test parameters that will make one application or dissemination technique more practical than another. As with the vapor contamination, it is extremely important to determine the initial and final surface contamination concentrations during a test, and the analytical procedures for liquid MS in paragraph 3.4 can be employed. A 250 µL or smaller syringe can be used to contaminate small items directly with a known quantity of liquid simulant.

3.6 Agent/Simulant Correlations.

Methyl salicylate is used as a trialing simulant for HD or 2,2 - Dichlorodiethyl sulfide. Depending on the test subject

of interest involving either the vapor hazard or contact hazard of HD, it is desirable that the chemical agent simulant used would have similar physical characteristics in those properties which influence the chemical/physical mechanism(s) associated with the hazard(s) under investigation. For example, molecular weight, melting point, boiling point, vapor density, and vapor pressure would be properties of particular interest for a simulant when investigating the vapor hazard of HD. In studying the liquid contact hazard or transfer characteristics of HD, the surface tension, spread factors, viscosity, and diffusion coefficient of the simulant would be properties of greater interest in comparison to those mentioned for a vapor hazard. The table below compares some of the physical properties between HD and MS.

Table 1. Comparison of Some Physical Properties Between MS and HD. (Long, Wallace[9])

Description of Property	MS	HD
Molecular Weight (g/mol)	152	159
Molecular Volume (cm^3/mol)	129	125
Melting Point (°C)	1	14
Boiling Point (°C)	223	217
Flash Point (°C) - Closed Cup	101	105
Saturation Concentration at 20 °C (mg/m^3)	7.57×10^2	6.09×10^2
Vapor Pressure at 20 °C (mmHg)	0.091	0.070
Liquid Density at 25 °C (g/mL)	1.18	1.27
Viscosity at 20 °C (cs)	8.26	4.50
Heat of Vaporization at 25 °C (cal/g)	89.4	90.8
Surface Tension at 25 °C (dynes/cm)	39.8	42.1
Solubility in Water (g/100 mL)	0.07 @30 °C	0.09 @22 °C
Solubility Parameters:		
1. Hildebrand (cal/cm^3)	10.6	10.0
2. H-bond (cal/cm^3)	6.0	4.0
Contact Angle on Dry Surface (degrees)		
1. Teflon	54	63
2. Silicone	44	57
3. Paraffin	47	50
4. Polyethylene	28	43
5. Lucite	20	15
6. Glossy White Polyurethane Paint	11	17
7. Matt Olive Polyurethane Paint	8	15
8. Rust Alkyd Undercoat Paint	33	25

The area spread or covered by a drop is determined by the drop volume and initial area contacted or wetted by the drop (measurable by the contact angle Θ, see Figure 1). The contact angle is a function of the liquid density, liquid surface tension and the acceleration of gravity (See Appendix D for more detailed information for estimating the spread of a liquid). It can be seen from the data in the table that MS does not spread the same way as HD does for most substances. MS spreads quite differently on a polyurethane painted surface when compared to an alkyd painted surface. Figure 2 shows this spread difference for MS on an alkyd painted surface and a chemical agent resistant-coated (a polyurethane painted) surface. MS can be thickened by adding Poly Methylmethacrylate (K125) to modify some of its properties to better approximate the spread of HD on some surfaces and other contact or liquid transfer characteristics (See Appendix E for the MSDS on K125).

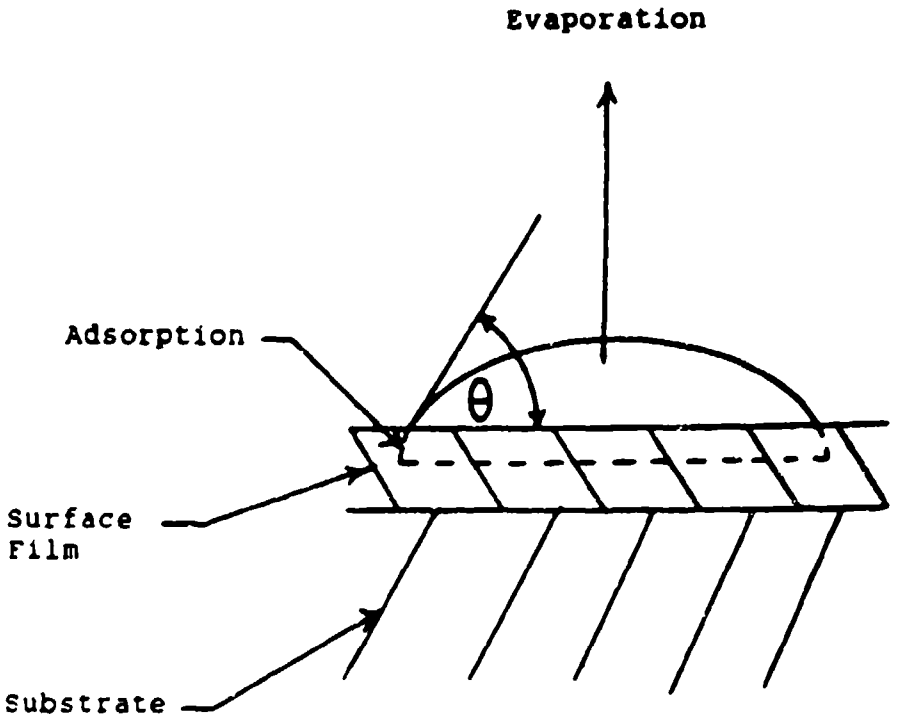

Figure 1 - Definition of a Contact Angle Formed By a Drop on a Surface

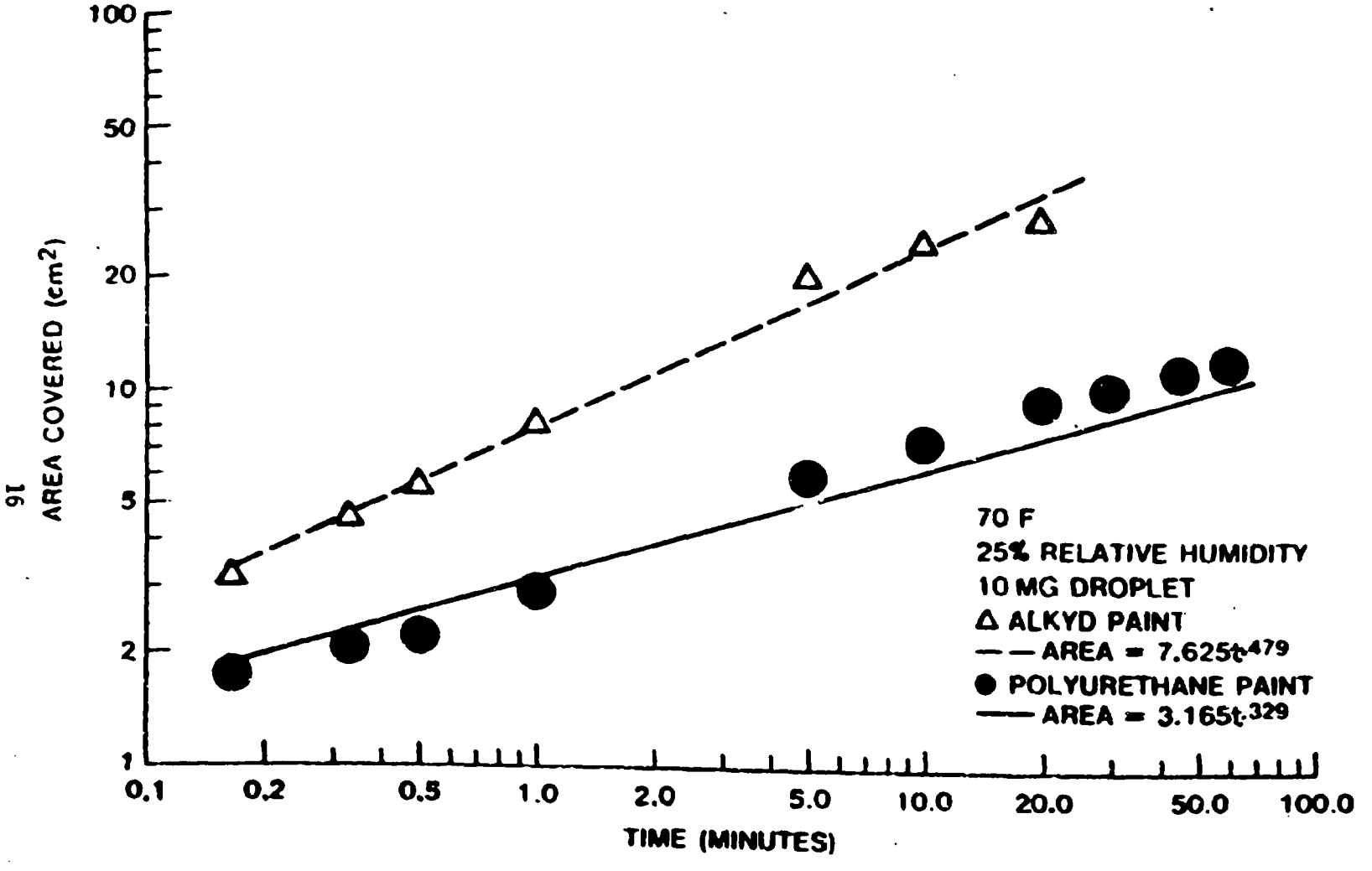

Figure 2. Spread of Methyl Salicylate on Alkyd and Polyurethane Painted Surfaces

3.7 Producibility.

Methyl salicylate is commercially available in industrial and analytical grades. It is manufactured by various chemical companies such as Monsanto Company located in St. Louis, Missouri and Bayer U.S.A., Inc./Mobay Corporation located in Pittsburgh, Pennsylvania.

3.8 Transportation/Storage/Disposal Information.

See Appendix B.

3.9 Chemical Stability/Material Compatibility Information.

See Appendixes B and C.

4. CONCLUSION

Methyl salicylate (MS) is a good overall mustard (HD) trialing simulant, especially in the investigation of the vapor hazards associated with HD. It has proven to be an excellent chemical agent simulant for HD in the use categories of hazard/threat, individual and collective protection, decontamination, and detection. In addition, MS is relatively safe to the environment and those personnel handling the liquid. The disposal of MS is also less costly and restrictive when compared to other simulants, because it is not considered a RCRA waste or a hazardous material. However, experimental measurements have been conducted on the spread of MS and HD on various coated surfaces, and it was noted that MS does not simulate the spread of HD on most surfaces. In particular, HD does not spread appreciatively on alkyd painted surfaces while MS spreads extensively. On chemical agent resistive coated (CARC) surfaces, both liquids spread, but MS spreads more slowly on a CARC surface than on an alkyd paint surface. So, this behavior would suggest that neat MS would not be an acceptable HD simulant where spreading and its related physical processes are critical. The evaporation of MS from paints will be unlike the evaporation of HD, because the area covered (spread) will be different even though their vapor pressures and evaporation rates are similar. Thickened MS approximates the spreading of HD much better than neat MS. In addition, MS has a strong wintergreen odor and depending on the manufacturer, it may be either clear, light yellow, or pink. Test personnel in MOPP IV gear should not smell the MS vapor if their masks are properly sealed, but if test personnel are not wearing a mask they will be able to smell MS in the area. The odor or color of MS may or may not make MS a suitable chemical agent simulant depending on the specific test requirements.

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APPENDIX A

METHYL SALICYLATE TOXICITY DATA EXTRACTED FROM LITTLE[1]

METHYL SALICYLATE

Methyl salicylate has the characteristic odor and taste of wintergreen. It is widely used in the perfume and food industries, as well as medicinally in the form of local analgesic or anti-inflammatory ointments or liniments (Collins et al., 1971). It was given GRAS status by the Flavor and Extract Manufacturers' Association (1965). The Food and Drug Administration proposed tolerances for methyl salicylate of 100 ppm in bakery goods, 300 ppm in candy, 70 ppm in carbonated beverages, 3300 ppm in chewing gum and 50 ppm in ice cream (Food Chemical News Guide, 1982). Methyl salicylate is also cleared for use in adhesives and as an antioxidant and stabilizer for semirigid and rigid acrylic and modified acrylic plastics (Food Chemical News Guide, 1982). Furia and Bellanca (1975) reported uses of 54 ppm in bakery goods, 840 ppm in candy, 59 ppm in non-alcoholic beverages, 8400 ppm in chewing gum, 27 ppm in ice cream and 200 ppm in syrups. The Eleventh Report of the Joint FAO/WHO Expert Committee on Food Additives (1968) reported an estimated acceptable daily intake for man of up to 500 µg/kg body weight.

Potential Health Effects

Human Data

- Acute Toxicity

Although methyl salicylate is considered safe for use as a flavoring agent in various foods when added in low concentrations, it has been found to be acutely toxic when ingested in relatively small but concentrated amounts. A dose of 30 ml concentrated methyl salicylate (~0.5 g/kg) may be fatal to adults, while as little as 4-10 ml may be fatal to infants or children, depending on the size and condition of the child (Stecher, 1968; Adams et al., 1957; Cann and Verhulst, 1958; Canselmo, 1948; Deichmann and Gerarde, 1969; Wade, 1977).

Symptoms of methyl salicylate poisoning are similar to those caused by other salicylates (i.e., sodium salicylate, acetylsalicylic acid) and may include nausea, vomiting, perspiration, marked thirst and dehydration, occasional diarrhea, acidosis, pulmonary edema, pneumonia, hyperpyrexia, hyperpnea, high blood pressure, increased heart rate, dimness of vision and excitation of the central nervous system. In severe cases, generalized convulsions and coma are followed by cardiovascular collapse and respiratory insufficiency leading to death within 12-36 hours after exposure (Adams et al., 1957; Stecher, 1968; Deichmann and Gerarde, 1969). In general, symptoms of salicylate poisoning become apparent with blood salicylate levels of approximately 25 mg/100 ml, severe intoxication in individuals with lower blood salicylate levels, however, is not uncommon (Cann and Verhulst, 1958; Deichmann and Gerarde, 1969).

Methyl salicylate poisoning is apparently due to the salicylate moiety, and not the methyl alcohol produced by hydrolysis of the ester in the stomach. Most clinical signs of methyl salicylate poisoning are attributable to changes in the acid-base balance and electrolyte structure of the plasma. Salicylate stimulation of the respiratory center produces hyperpnea and results in a CO_2 deficit in blood, decreased carbonic acid content and a rise

in blood pH (i.e., respiratory alkalosis). Renal compensation by increased bicarbonate excretion facilitates the development of acidosis. Another contributing factor to acidosis is a salicylate-induced change in carbohydrate metabolism which causes an abnormal production and accumulation of organic acids. The removal of these abnormal metabolic end-products results in the excretion of fixed base. Salicylates have been shown to inhibit the first two steps in the Kreb's tricarboxylic cycle, resulting in ketosis which may contribute to the acidosis. The diaphoresis and hyperpnea produced by the salicylate moiety cause water loss from the body, which is increased by coincident vomiting and diarrhea. This leads to body water deficit with impaired renal function and decreased salicylate excretion. Salicylate poisoning may also cause hypoprothrombinemia, leading to depression of plasma fibrinogen and widespread capillary damage (Cann and Verhulst, 1958; Adams et al., 1957). Hyperlactatemia and hyperkalemia were observed in patients who subsequently died from myocardial failure following accidental ingestion of ~30-90 ml of methyl salicylate. Autopsy revealed myofibrillar necrosis which was most marked in the subendocardial region of the left ventricle (Ojiambo, 1971b).

- Dermal Effects

Methyl salicylate is a strong dermal and mucous membrane irritant and is readily absorbed through the skin. Although it is considered to be too irritating for internal use, methyl salicylate has been frequently employed as a topical counterirritant, analgesic and/or anti-inflammatory agent. It is used both undiluted or in various ointments, liniments and lotions for relief of pain, stiffness and inflammation of sciatica and rheumatic conditions (Wade, 1977; Tilley, 1980; Deichmann and Gerarde, 1969; Davison et al., 1961). When applied to the skin, the resulting irritation reportedly interferes with the transmission of impulses from local pain fibers. Tilley (1980) urged that caution should be taken to avoid application to the eyes or mucous membranes because of potential severe irritation and to avoid application to irritated skin, wounds or large areas of the body because of potential toxicity resulting from systemic absorption.

Although Morgan (1968) reported sensitivity to methyl salicylate confirmed by patch tests in 2 patients, Epstein (1973) reported no irritation and no sensitization after application of methyl salicylate (8% in petrolatum) for 48 hours with occlusion.

- Hemolytic Effects In Vitro

Two studies reported significant hemolysis in human red blood cells incubated with methyl salicylate at concentrations as low as 0.004 ml (in 5 ml solution). The hemolytic effect was concentration- and time-dependent with maximum effects seen with 60 minutes exposure to 0.01 ml. Methyl salicylate appears to cause hemolysis, even at very low concentrations, by reducing the surface tension, resulting in damage to the erythrocyte membrane (Muragesh, 1981a). This was further substantiated by the effective and significant antagonism of the methyl salicylate-induced hemolysis by addition of a variety of drugs to the cell suspension; these included urethane, histamine acid phosphate, procaine hydrochloride, acetazolamide and

tetracycline hydrochloride. Hemolysis was decreased approximately 70% by the simultaneous addition of 1 x 10^{-3} M antagonist and 1 x 10^{-3} M methyl salicylate to the red blood cells or by the initial incubation of cells and antagonist, prior to addition of methyl salicylate. Although the exact mechanism of this protective effect is not known, it was suggested that complexes or interactions between the methyl salicylate and the drugs led to inactivation of the methyl salicylate, thus preventing the lowering of the surface tension and the resulting membrane damage (Muragesh, 1981b).

- Cytotoxicity

At concentrations of 1, 10 or 100 µg/ml, methyl salicylate was not cytotoxic to HeLa cell cultures (Silyanovska et al., 1968).

Animal Studies

- Acute and Subchronic Toxicity

LD_{50} values for a number of different species have been reported (Updyke, 1978b; Stecher, 1968; Sax, 1979; RTECS, 1980) as follows:

Species	Oral LD_{50} (mg/kg)	Dermal LD_{50} (mg/kg)
mouse	1100	
rat	887, 1250	
guinea pig	700, 1060	
rabbit	1300, 2800	>5000
dog	2100	

Administration of 0.5 ml methyl salicylate by gavage caused slight redness and irritation of the stomach mucosa of rats (Strom and Jun, 1974). In another study, however, methyl salicylate was found to have markedly less acute gastric ulcerogenic activity compared to salicylic acid when administered orally to rats. Groups of 4-6 animals were given a 1 ml suspension of methyl salicylate in water, or the same dose of salicylic acid, followed by a brief exposure to the cold (1-15°C for 45 minutes) as a stress-sensitizing procedure. The number of gastric lesions was reduced from 4.8 ± 1.9 with salicylic acid to zero with methyl salicylate. This reduction in ulcerogenic activity was apparently not accompanied by any anti-inflammatory activity. In the same study, oral administration of methyl salicylate was also notably more effective than salicylic acid in significantly reducing fever induced in rats by subcutaneous injection of 2 g/kg dried Brewer's yeast in saline (Rainsford and Whitehouse, 1980; Whitehouse and Rainsford, 1980).

Administration of 0.6-4.7 g/kg methyl salicylate by intubation into the stomach and duodenum of 4 dogs caused nausea, vomiting, diarrhea, intense hyperpnea, excitation of the central nervous system and death in two animals at 8 and 18 hours, respectively. An increase in respiratory amplitude but no change in arterial pressure were noted when anesthetized dogs were given 0.5-5 g/kg methyl salicylate (Lacroix and Ferragne, 1964).

Ojiambo (1974), however, reported a drop in blood pressure and cardiac output and a slight increase in heart rate within 5 hours after intragastric administration of 0.7 g/kg methyl salicylate to dogs. Methyl salicylate-induced changes in various metabolic parameters were thought to be responsible for resulting myocardial failure and skeletal (hind limb) muscle necrosis; these included increased levels of creatine phosphokinase (CPK) in coronary effluent and skeletal muscle bed, a marked net efflux of both K^+ and lactate from the muscle bed, and a steady rise in oxygen consumption. It was concluded that hyperkalemia was produced by a methyl salicylate-induced uncoupling of oxidative phosphorylation, which caused a reduction in the level of high energy phosphate necessary to maintain the normal muscle cell membrane potential, thus altering the transport of K^+. The exact mechanism and site of uncoupling was not determined (Ojiambo, 1971b,d). Ojiambo (1971a) also suggested that increased arterial levels of catecholamines (epinephrine and norepinephrine) in dogs intoxicated by methyl salicylate may have been a factor in the skeletal and cardiac cell damage.

In a subchronic feeding study, Webb and Hansen (1963) observed growth retardation but no gross or microscopic abnormalities in 20 rats fed 10,000 ppm methyl salicylate in the diet (1%) for 17 weeks. No effects were observed in rats fed 1,000 ppm (0.1%). Harrison et al. (1963) reported an increase in cancellous (i.e., spongy) bone in the femurs and tibias of rats fed 20,000 or 11,250 ppm methyl salicylate in the diet for 10 weeks, while no effects were observed with levels of 2,000 3,550, 6,330 or 9,000 ppm.

Weight loss and death within a month were observed in pairs of dogs given daily capsules of 500, 800 or 1200 mg/kg methyl salicylate 6 days/week. At the two highest dosage levels, moderate to marked amounts of fatty metamorphosis were noted in the liver. No adverse effects were noted in 8 dogs given daily capsules of 50, 100 or 250 mg/kg, 6 days/week for up to 59 days (Webb and Hansen, 1963).

Anorexia, weight loss, depression and death in 6-28 days occurred in 3 rabbits after application to the clipped back with 4 ml/kg/day methyl salicylate, 5 days/week. In one case, microscopic examination of tissue showed several distinct lesions indicative of kidney damage. Applications of 2, 1 or 0.5 ml/kg/day, 5 days/week for up to 96 days resulted in a slight to very slight dermatitis and an increased incidence of spontaneous nephritis and mild hepatitis. Two of 3 rabbits treated with 2 ml/kg/day showed a slight sloughing of the epidermal scales (Webb and Hansen, 1963).

Gage (1970) reported no signs of toxicity or organ abnormalities in rats after twenty 7-hour exposures to saturated methyl salicylate vapor (120 ppm, 700 mg/m^3).

- Chronic Toxicity

In a 2-year feeding study, growth retardation, rough coats and death within 49 weeks were observed in 50 rats fed 20,000 ppm methyl salicylate in the diet (2%). Pneumonia was the only obvious gross lesion, occurring in 29/50 (58%) of the treated animals; this condition was more acute and resulted in more lung abscesses in the treated rats compared to control rats. Although no other gross lesions were apparent, it must be noted that all the treated rats died before the usual age at which spontaneous lesions develop.

Hematological analyses were negative, while microscopic examination revealed an excess of cancellous tissue in the bone. Addition of 10,000 ppm methyl salicylate to the diet (1%) for 2 years caused growth retardation and rough coats. Both 10,000 ppm (1%) and 5000 ppm (0.5%) in the diet caused a slight excess in cancellous tissue in the bone. No gross or microscopic effects were noted with addition of 1,000 ppm (0.1%) (Webb and Hansen, 1963).

In the same study, weight loss and growth retardation were noted in 7 dogs given daily capsules of methyl salicylate (150 or 350 mg/kg/day), 6 days/week for 2 years. Gross examination revealed enlarged livers, and microscopic examination showed enlarged hepatic cells, but no excess fatty metamorphosis. No effects were noted in 4 dogs dosed with 50 mg/kg/day for 2 years (Webb and Hansen, 1963).

- Skin Irritation/Sensitization

A number of studies have reported various dermal effects of methyl salicylate applied to rabbit, rat or guinea pig skin. Moreno (1973) found methyl salicylate to be a moderate irritant to intact or abraded rabbit skin when applied full strength for 24 hours under occlusion. Similarly, Yankell (1972) noted mild to moderate irritation following application of 1,3 or 6% methyl salicylate in several different vehicles to intact rabbit skin (shaved and depilated) for 24-72 hours with occlusion (Saran® wrap). Results were as follows:

	Irritation Index*		
	methyl salicylate concentration		
Vehicle	1%	3%	6%
H_2O suspension	-	0.83 (mild)	1.83 (mod.)
PEG 400	0.33 (mild)	0.50 (mild)	0.50 (mild)
70% ethanol	1.17 (mild)	4.17 (mod.)	4.00 (mod.)
70% ethanol with emollients	2.17 (mod.)	3.00 (mod.)	3.00 (mod.)

* According to the Draize Method

Slight erythema and edema were noted after 24 hours with 1% methyl salicylate in 70% ethanol, while necrosis was observed with the 3% and 6% formulations. Necrosis and intradermal and subcutaneous hemorrhage were produced with all three concentrations of methyl salicylate in 70% ethanol with emollients. Polyethylene glycol (PEG) reportedly inhibits the penetration of methyl salicylate into the skin and/or decreases its release from solution. Similarly, the addition of emollients has been reported to cause release of only a part of the total amount of methyl salicylate from an ethanol solution.

In a skin sensitization test, methyl salicylate caused no significant allergic reactions in guinea pigs. Twenty animals received one intracutaneous injection of 0.1% methyl salicylate in Freund's adjuvant and saline every other day for 3 weeks for a total of 10 applications. Fourteen days after the last injection, a challenge dose of 1 ml of 0.1% methyl salicylate was administered by intradermal injection. Positive allergic

reactions were noted in 2/20 (10%) treated animals compared to 0/20 in controls ($P>0.01$). A second challenge dose of methyl salicylate, administered 10 days later by the epidermal route, consisted of a maximal subirritant concentration (10%) applied in soft white petrolatum under occlusive dressings for 24 hours. No allergic reactions were observed in any of the 20 treated animals (Maurer et al., 1980).

- Hematological Effects

Salicylates have been known to interfere with the synthesis of vitamin K_1-dependent clotting factors VII, IX and X, and also to prolong prothrombin time in vitamin K_1-deficient rats and rabbits. Park and Leck (1981) observed significant decreases in prothrombin complex activity (PCA) and in levels of vitamin K_1-dependent clotting factors II, VII and X (but not V) in rabbits following intramuscular injection of 1 g/kg methyl salicylate (in a split dose). Despite this high dose, recovery of normal plasma PCA occurred after about 30 hours, or within 2 hours if 2 mg/kg vitamin K_1 was administered intravenously. The reappearance of PCA was directly related to plasma salicylate levels, with total suppression of the synthesis of PCA (indicating complete inhibition of clotting factor synthesis) occurring at a minimum salicylate level of 355 ± 12 µg/ml. The data indicated that methyl salicylate elicited its effect on the vitamin K_1-epoxide cycle at the epoxide reductase step, thus preventing regeneration of vitamin K_1 and causing a reduction in clotting factor synthesis. Although salicylates are not known to produce hypothrombinemia at normal therapeutic doses, the authors suggested that such an effect could occur with an overdose or with a normal dose taken simultaneously with another drug which affected vitamin K_1 concentrations in the liver.

- Reproductive Effects/Teratogenicity

A number of studies have reported increased incidences of teratogenic effects in rats and hamsters following induction of methyl salicylate poisoning in pregnant dams during the early stages of embryonic development. To our knowledge, however, congenital malformations attributable to methyl salicylate or salicylate intake by the mother have not been recorded in man.

Single subcutaneous injection of 0.1 ml methyl salicylate to pregnant rats on day 10 or 11 of gestation resulted in incidences of fetal resorption of 27.3 and 32.7%, respectively, and fetal abnormalities in 31.4 and 18.2%, respectively, of the live births. Most abnormalities involved the cardiovascular, urogenital and/or skeletal systems. Retarded fetal growth, abnormalities of the branchial arch arterial derivatives, cleft lip, cleft palate and hydroureter were commonly seen; "club-foot" and phocomelia of the hind-limbs were frequently seen after injection on day 11. Hydronephrosis, ectopic kidneys, and exencephaly were occasionally observed. Greater frequencies of resorption and fetal abnormalities were apparent when administration of methyl salicylate was combined with hypoxia for 6 hours (25,000 feet altitude equivalent). It was suggested that hypoxia aggravated the increased utilization of oxygen by the tissues which was induced by the methyl salicylate (Bertone and Monie, 1965).

Warkany and Takacs (1968) observed even higher incidences of abnormalities in rats following single subcutaneous injections of 0.1-0.5 ml

methyl salicylate to 116 pregnant dams on days 9, 10 or 11 of gestation. Results of treatment included 26 maternal deaths (22.4%), 47 resorptions (40.5%) and 120 fetal abnormalities among 298 live births (40.3%). No fetal abnormalities were noted in 484 live births from 59 untreated controls. Congenital malformations included 4 cases of exencephaly, 4 cases of hydrocephalus and 9 cases of harelip, oblique facial clefts and/or cleft palate. Some anomalies of the vertebrae and ribs were noted, while in only 2 cases were the bones of the extremities grossly deformed. Of special note in this study was the occurrence of 12 cases of craniorachischisis, a congenital fissure of the skull and spinal column; 5 of these 12 also had gastroschisis with protrusion of the stomach, liver and intestine. This condition was thought to be comparable to early stages of craniorachischisis in humans (Warkany and Takacs, 1968).

In an extension of the above study, using the same methods, Takacs and Warkany (1968) observed induction of cardiovascular malformations in 30/159 (18.9%) fetuses removed on day 21 of gestation from methyl salicylate-treated dams. The most common abnormality was transposition of the aorta to the right, with displacement ranging in degree from "overriding aorta" to complete transposition. In addition, there were 2 cases of isolated ventricular septal defects and two dextrocardias.

Similarly, Woo and Hoar (1971, 1972) found that intraperitoneal injection of 0.05 or 0.1 ml methyl salicylate to pregnant rats on days 10 or 11 of gestation caused a retardation in renal development, particularly growth of renal papilla. During the normal pattern of renal development in the rat fetus the renal papilla increase slowly and steadily in length, while the renal parenchyma increases rapidly and almost exponentially in weight, resulting in an abnormally large renal pelvis and "apparent hydronephrosis" late in gestation. This apparent abnormality decreases by steady lengthening of the renal papilla with advancing fetal and postnatal age, and generally disappears shortly after birth. Treatment of pregnant females with methyl salicylate appeared to inhibit the lengthening of the renal papilla and caused reduced kidney weights through some effect on renal growth. This resulted in an increased number of kidneys with an apparently enlarged renal pelvis. In addition, a higher frequency of fetuses from treated dams had kidneys with no papilla at all. Some recovery from methyl salicylate-induced effects was apparent, with kidney weights and renal papillary lengths nearly normal by postnatal day 6. However, gross dilation of the renal pelvis, reduction of renal parenchyma, and papilla of narrower circumference (although of normal length) were noted in 11/138 (8%) of the treated fetuses at weaning. This persistent condition, suggestive of hydronephrosis or hypoplasia, was not noted in control fetuses.

Monie (1970) noted occurrences of hydronephrosis and hydroureter in fetuses from similarly treated rats. In some cases these abnormalities were associated with an obstruction or structural aberration in the urinary tract, while in some, the urinary tract was unobstructed and terminated normally. In the latter cases, the dilatation may have been a result of neuromuscular imbalance. In all cases, there was a reduction in the number of glomeruli and retarded development of the renal tubules; usually the collecting tubules were dilated and shortened.

A variety of reproductive effects were noted when groups of 20 rats were fed 500, 1,500, 3,000 or 5,000 ppm methyl salicylate in the diet for 3 generations. Although no significant decrease was observed in the fertility index at any dosage level or generation, notable decreases were observed in average litter size, average number of liveborn progeny, viability index, the number of progeny surviving 4 days and the number surviving to weaning at dose levels of 3,000 and 5,000 ppm methyl salicylate. These decreases were most significant in the second generation. Combined results from all 3 generations indicated an apparent dose-related response, starting at 1500 ppm, in the average litter size, number of liveborn progeny and the number of day 4 survivors. No grossly visible abnormalities were observed in external examinations of newborns or weanlings from any generation; autopsies and histological examinations of third generation weanlings revealed no abnormalities or evidence of toxicity (Collins et al., 1971).

Both topical and oral administration of methyl salicylate to pregnant hamsters on day 7 of gestation reportedly resulted in failure of neural tube closure in nearly 75% of the embryos recovered at day 9. However, in order for topical administration to result in blood salicylate levels equal to those caused by oral administration, a topical dose more than 8 times larger than the oral dose was necessary (~14 g/kg compared to 1.75 g/kg methyl salicylate). Also, the level of salicylates in the blood increased much more gradually following topical application compared to oral administration, with maximum levels occurring at 5-6 hours and 2 hours, respectively. The authors suggested that although absorption of methyl salicylate through the hamster skin could induce teratogenic effects similar to those obtained after oral treatment, the response required very large topical doses (Overman, 1979; Overman and White, 1978).

White (1978) reported that variations in the teratogenic response in hamsters to methyl salicylate was affected by differences in fetal age which apparently correspond to different intrauterine positions. When pregnant hamsters were given oral doses of 175-225 mg methyl salicylate per 100 g body weight at specific times during the period of gestation from day 7 hour 9 to day 7 hour 22, the frequency of cranium bifida in embryos at day 9 ranged from 16-73%, compared to 11% in controls. The critical importance of timing was indicated by the fact that treatment at hour 21 resulted in a significant frequency of defects, while treatment just one hour later, at hour 22, induced a frequency of defects not statistically different from the control value.

Szabo et al. (1971) reported that methyl salicylate was embryotoxic and teratogenic in both mice and rabbits when administered during pregnancy (doses, route and time of administration not stated). Malformations included cleft palate, exencephaly, hydrocephalus, amphalocele, open eyelid and spina bifida.

It should be noted that the doses of methyl salicylate which induced teratogenic effects in these studies were close to dose levels which are lethal to the embryo and toxic to the dam, thereby decreasing the expected yield of offspring. Also these doses were, on a weight basis, far greater than therapeutic human doses. Takacs and Warkany (1968) estimated that an

equivalent dose in humans to that inducing a teratogenic response in rats would require intake of approximately 30 g of salicylates ingested by a 60 kg female during early gestation.

- Carcinogenicity

No increase in the incidence of lung tumors was noted in strain A mice given 24 intraperitoneal injections of a maximum tolerated dose of methyl salicylate or 20% of this dose over an 8 week period; the actual doses administered were not stated (Stoner et al., 1973).

Metabolic Characteristics

Human Data

Methyl salicylate is rapidly absorbed through intact human skin or by ingestion. It is hydrolyzed in the stomach to methyl alcohol, and salicylic acid which is converted to sodium salicylate in the intestine and absorbed. Although largely hydrolyzed, it is also absorbed, at least in part, as the intact ester. Methyl alcohol is seldom produced in sufficient quantities to be a factor in intoxication; approximately 75% of the methyl salicylate is available as salicylate (Gosselin et al., 1976; Adams et al., 1957).

Salicylate is rapidly distributed throughout all body fluids and can be detected in synovial, spinal and peritoneal fluid, saliva, bile and milk. The intact ester is also hydrolyzed in the plasma and tissues to salicylic acid and its metabolites. Approximately 70-80% of the salicylate in human plasma is bound to non-diffusible components, presumably plasma protein. Salicylates are excreted in the urine in the form of salicylates or their metabolites. Small amounts of unhydrolyzed ester may also be excreted, giving the urine a slight odor of wintergreen (Adams et al., 1957).

Maruta and coworkers (1977) observed peak serum concentrations of free salicylic acid (4 µg/ml) and total salicylates (12.5 µg/ml) 8 and 12 hours, respectively, after initiation of a single 12-hour application to the backs of human volunteers of 10 plasters, each containing 350 mg methyl salicylate and covered with plastic film. Levels of salicylates were negligible at 24 and 48 hours after application. Urinary excretion of total salicylates reached a plateau of approximately 37 percent 24 hours after application. with little to no free or total salicylates measured in the urine by 36-48 hours. Following repeated 12-hour applications, each 12 hours apart, for 6 days, only trace to no free salicylic acid or total salicylates were detected 12 hours after removal of the 2nd, 4th or 6th plaster and no salicylates were detected 36 hours after the last (6th) application. Thus, salicylates did not appear to accumulate in the human body at this dose level, even with repeated application.

Several studies have indicated that hydrolysis of methyl salicylate in humans is slower and of lower magnitude than that seen in dogs or rats. An appreciable amount of unhydrolyzed methyl salicylate was measured in plasma 15 minutes (39%) and 90 minutes (21%) after ingestion of 0.42 ml methyl salicylate in ginger ale. Total plasma salicylate concentrations were significantly less than those obtained after similar administration of acetylsalicylic acid. In tests with dogs, negligible amounts of methyl

salicylate were measured in the total plasma salicylates within 60 minutes after oral administration of a much higher dose than that administered to humans (equivalent to ~300-500 mg/kg salicylic acid compared to ~7 mg/kg). Other reports have also indicated that lethal concentrations of total circulating plasma salicylates in man were 2-3 times higher than those in dogs at the time of death. It has been suggested that large doses of methyl salicylate administered to humans could overwhelm an apparently inadequate detoxification mechanism, resulting in even less hydrolysis, greater uptake of the highly lipid-soluble undissociated ester by such tissues as the brain, and a consequent increase in toxicity. In 3 cases of accidental ingestion of ~30-90 ml of methyl salicylate, about 21% of the dose was still circulating in the plasma at the time of myocardial failure (Ojiambo, 1971c; Davison et al., 1961).

Animal Studies

Absorption of topically applied methyl salicylate was shown to be quite rapid in mice and rabbits. High levels of radioactivity were measured in the skin of hairless mice at the exposure site within 1 hour after percutaneous application of a plaster containing 127 mg/kg [^{14}C]-labelled methyl salicylate for 1, 2, 4, 8, 12, 24 or 48 hours. Levels of activity peaked at 4 hours, then gradually decreased until virtually no activity was measured at 48 hours. Only slight radioactivity was detected in the skin adjacent to the application site at 2 and 4 hours. Serum levels of radioactivity peaked (equivalent to 15 µg/ml salicylates) 2 hours after application, then decreased gradually. Cumulative urinary excretion of radioactivity was 33.5 and 39.3% of the dose in mice treated for 24 and 48 hours, respectively. It appeared that the methyl salicylate was absorbed rapidly from the plaster and was localized at a high concentration in the skin at the application site (Maruta et al., 1977).

Kitagawa and coworkers (1979b) noted an even higher rate of absorption of radiolabeled methyl salicylate when applied to rabbit skin. Radioactivity was detected in the blood 15 minutes after application and peaked at 2 hours after administration. Distribution of methyl salicylate was widespread, with radioactivity observed in nearly all organs and tissues. Excretion was also rapid, with total radioactivity (32.88% of the dose) eliminated in the urine at 94 hours; no radioactivity was found in the feces.

Kida (1978) found that percutaneous absorption of methyl salicylate from the back of rabbits, pigs and humans could be increased by raising the temperature of the methyl salicylate-containing poultice.

Several studies have indicated that more extensive hydrolysis of methyl salicylate occurs in the intestine after oral administration compared to other routes of administration. Williams (1959) reported that only 0.2-0.5% of an oral dose of 0.2 g/kg appeared unchanged in the urine of dogs, while 14% of the dose appeared unchanged in the urine after intramuscular injection. Similarly, Davison et al. (1961) noted from plasma analyses that hydrolysis was about 95% complete at 1 and 4 hours in dogs given capsules (orally) of 300 mg/kg methyl salicylate. Ojiambo (1971a) observed an initial 1 hour delay in the absorption of methyl salicylate, followed by a steady linear rise in plasma salicylate levels up to 3 or 4 hours after intragastric administration of 700 mg/kg methyl salicylate to dogs. No

further significant increase in blood salicylate levels was observed after 3 hours in dogs surviving the treatment or after 4 hours in dogs dying within the study period. The data indicated a higher rate of absorption and/or a slower rate of elimination in the dogs that died within 5 hours of treatment (3 of which had received an additional 100 mg/kg methyl salicylate 2 hours after the first dose). The initial delay in appearance of salicylate in the blood was attributed to a delay in passage of methyl salicylate into the small intestine from the stomach, possibly due to spasm of the pylorus caused by gastric irritation. Once absorption was initiated, hydrolytic and detoxification mechanisms converted the methyl salicylate to its metabolites. Ojiambo (1971c) also indicated that the level of total plasma salicylates which resulted in death of female dogs was lower than that of male dogs.

In a similar study, plasma and brain tissue analyses from rats demonstrated negligible amounts of methyl salicylate 20 and 60 minutes after administration by oral catheter of a dose equivalent to 500 mg/kg salicylic acid. Thus, hydrolysis of this near lethal dose was almost complete in as little as 20 minutes (Davison et al., 1961).

Monitoring and Detection

Methyl salicylate would be rapidly converted by esterases to salicylic acid (o-hydroxybenzoic acid). The metabolites of salicylic acid include salicyluric acid (glycine conjugate), the acyl and phenolic glucuronides, gentisic acid and gentisuric acid. Salicyluric acid would be the major metabolite (~80%) in urine. Salicylic and salicyluric acids may be readily analyzed in either plasma or urine samples by high performance liquid chromatography (Sadee and Beelen, 1980). The assay is sensitive to 0.5 µg/ml for both compounds. A gas chromatographic procedure is reported for the analysis of methyl salicylate in either plasma or urine; however, the method is based on 20 µg of compound/ml plasma (Pentz and Schutt, 1978). This concentration is much higher than can be expected under simulant training conditions. Acetylsalicylic acid (aspirin) would give the same metabolic products as the salicylate esters. Therefore, unless the salicylate esters can be detected in plasma, urine or saliva, military personnel would have to forego use of aspirin as a pain reliever prior to any military exercise.

Possible qualitative tests for the detection of salicylate esters on either clothing or equipment include ultraviolet light and 5% aqueous ferric chloride spray (greenish-blue color) (Walash and Hassan, 1978).

APPENDIX B

MATERIAL SAFETY DATA SHEET FOR METHYL SALICYLATE

APPENDIX B

Mallinckrodt
Material Safety Data

Emergency Phone Number: 314-982-5000

Mallinckrodt, Inc., Science Products Division, P.O. Box M, Paris, KY 40361.

METHYL SALICYLATE

PRODUCT IDENTIFICATION:

Synonyms: O-Hydroxybenzoic acid, methyl ester; synthetic wintergreen oil; salicylic acid, methyl ester

Formula CAS No.: 119-36-8

Molecular Weight: 152.13

Chemical Formula: $C_8H_8O_3$

Hazardous Ingredients: Not applicable.

PRECAUTIONARY MEASURES

WARNING! HARMFUL IF SWALLOWED, INHALED OR ABSORBED THROUGH SKIN. CAUSES IRRITATION.

Avoid breathing dust.
Keep container closed.
Use with adequate ventilation.
Avoid contact with eyes, skin and clothing.
Wash thoroughly after handling.

EMERGENCY/FIRST AID

If swallowed, induce vomiting immediately by giving two glasses of water, or milk if available and sticking finger down throat. Never give anything by mouth to an unconscious person. If inhaled, remove to fresh air. Get medical attention for any breathing difficulty. In case of contact, immediately flush skin or eyes with plenty of water for at least 15 minutes. In all cases call a physician.
SEE SECTION 5.

DOT Hazard Class: Not Regulated

SECTION 1 Physical Data

Appearance: Clear, practically colorless liquid.

Odor: Characteristic odor.

Solubility: Sparingly soluble in water.

Boiling Point: 222.2°C (432°F)

Melting Point: -8.3°C (17.1°F)

Specific Gravity: 1.180-1.185

Vapor Density (Air=1): 5.24

Vapor Pressure (mm Hg): 1 @ 54°C (129.2°F)

Evaporative Rate: No information found.

SECTION 2 Fire and Explosion Information

Fire:
Moderate fire hazard when exposed to heat or flame. Flashpoint: 101.1°C (214°F)
Autoignition point: 454.4°C (850°F)

Explosion:
Above the flash point, explosive vapor-air mixtures may be formed.

Fire Extinguishing Media:
Dry chemical, foam or carbon dioxide.

Special Information:
In the event of a fire, wear full protective clothing and NIOSH-approved self-contained breathing apparatus with full facepiece operated in the pressure demand or other positive pressure mode. Water spray may be used to keep fire exposed containers cool.

SECTION 3 Reactivity Data

Stability:
Stable under ordinary conditions of use and storage.

Hazardous Decomposition Products:
When heated to decomposition, emits acrid smoke and fumes.

Hazardous Polymerization:
This substance does not polymerize.

Incompatibilities:
Can react with oxidizing materials.

SECTION 4 Leak/Spill Disposal Information

Ventilate area of leak or spill. Clean-up personnel require protective clothing and respiratory protection from dust.

Spills: Pick up and place in a suitable container for reclamation or disposal in a method that does not generate dust.

Disposal: Whatever cannot be saved for reclamation may be disposed in a RCRA approved hazardous waste facility.

Ensure compliance with local, state and federal regulations.

NFPA Ratings: Health: 1 Flammability: 1 Reactivity: 0

Effective Date: 10-10-85

SECTION 5 Health Hazard Information

A. EXPOSURE / HEALTH EFFECTS

Inhalation:
Irritation of respiratory tract may occur. Can be a route for absorption into the body.

Ingestion:
Ingestion of absorbs amounts can cause "salicylism", as evidenced by abdominal pain, vomiting, increased respiration, and mental disturbances. Fatalities resulting from respiratory or cardiovascular failure are known. Reported lethal dose in human adult of 30 mls.

Skin Contact:
May cause irritation, and skin rashes in sensitive individuals. Skin absorption has reportedly occurred, but toxic levels are reached only when large skin areas are covered with the drug in a suitable base (e.g., lanolin).

Eye Contact:
Irritant to eye and surrounding membranes. Can be severe with permanent damage.

Chronic Exposure:
Central nervous system disturbances: such as rapid breathing, confusion and even convulsions may develop. Kidneys and pancreas can be affected by prolonged ingestion.

Aggravation of Pre-existing Conditions:
Persons with pre-existing skin disorders or eye problems, or impaired kidney or respiratory function may be more susceptible to the effects of the substance.

B. FIRST AID

Inhalation:
If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician.

Ingestion:
If swallowed, induce vomiting immediately by giving two glasses of water, or milk if available and sticking finger down throat. Call a physician immediately. Never give anything by mouth to an unconscious person.

Skin Exposure:
Remove any contaminated clothing. Wash skin with soap or mild detergent and water for at least 15 minutes. Get medical attention if irritation develops or persists.

Eye Exposure:
Wash eyes with plenty of water for at least 15 minutes, lifting lower and upper eyelids occasionally. Get medical attention immediately.

C. TOXICITY DATA (RTECS 1982)

Oral rat LD50: 887 mg/kg. Irritation data: skin rabbit 500 mg/24 Hr Moderate; eye rabbit 500 mg/24 Hr Severe Reproductive effects published data.

SECTION 6 Occupational Control Measures

Airborne Exposure Limits:
None established.

Ventilation Systems:
A local exhaust system which captures the contaminant at its source is recommended to prevent dispersion of the contaminant into the workroom air.

Personal Respirators (NIOSH Approved):
For conditions of use where exposure to the vapor is apparent, a half mask chemical cartridge respirator may be worn. For emergencies, a self- contained breathing apparatus may be necessary.

Skin Protection:
Wear impervious protective clothing, including boots, gloves, lab coat, apron or coveralls to prevent skin contact.

Eye Protection:
Use chemical safety goggles and/or a full face shield where splashing from solutions is possible. Contact lenses should not be worn when working with this material. Maintain eye wash fountain and quick-drench facilities in work area.

SECTION 7 Storage and Special Information

Keep in a tightly closed container. Store in a cool, dry, ventilated area away from sources of heat or ignition. Protect against physical damage.

MSSAL

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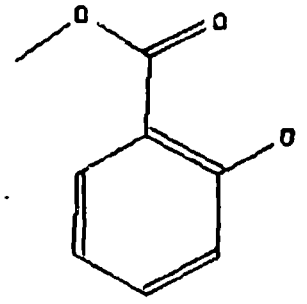
APPENDIX C

CHEMICAL/PHYSICAL/ENVIRONMENTAL INFORMATION ON METHYL SALICYLATE*

*Environmental Fate and Effects: Methyl Salicylate, CRDEC Data Management System, U.S. Army Chemical Research, Development and Engineering Center, Aberdeen Proving Ground, MD, 1987, UNCLASSIFIED Data Report.

CHEMICAL AGENT SIMULANT DATA CENTER

Entry Number 194	**Structure**  METHYL SALICYLATE
CRDEC Number CRDEC-0194	
CAS Reg Number 000119-36-8	
Formula C8 H8 O3	
Molecular Weight 152.151	
WLN QR BVQ1	**Synonyms** wintergreen oil 2-hydroxybenzoic acid methyl ester
Today's Date 02/26/88	
Page 1 of 5	

CHEMICAL AGENT SIMULANT DATA CENTER

METHYL SALICYLATE

Vapor Pressure [torr]
0.13 @20C Ref 55
0.165 @25C Ref 53
0.891 @28C Ref 79
1.0 @54C Ref Chem Eng Hnbk
40.0 @126.2C Ref Chem Eng Hnbk
400.0 @197.5C Ref Chem Eng Hnbk

Density [gm/cc]
1.1739 @20C Ref 55,64
1.182 @25C Ref 79

Boiling Point [C]
220.0 - 224.0 @760 Ref 42,55,64
222.9 @760 Ref 79

Surface Tension [dynes/cm]
38.8 @25C Ref 79

Vapor Density
5.24 Ref 55,64

Molar Vol.
128.94

Melting Point [C]
-8.6 Ref 42,64

Calc Molar Ref
39.58 Ref 85

Viscosity [cp]
9.7 @28C Ref 64 est

Volatility [mg/m3]
1060.0 @25C Ref 54
556.0 @28C Ref 79

Diffusivity [cm2/sec]

Refractive Index
1.5365 @28C Ref 42

Entry Number 194

CHEMICAL AGENT SIMULANT DATA CENTER

METHYL SALICYLATE

Heat of Vaporization [cal/gm]

89.4 @25C Ref 79
83.2 Ref 53

Heat of Combustion [cal/gm]

8986.0 Ref 53

Heat of Fusion [cal/gm]

Heat of Formation [cal/gm]

Energy to Vaporize [cal/gm]

Heat Capacity [cal/gm degC]

Specific Heat [cal/gm]

Decomp Temp [C]

Oxygen Index

Flash Point [C]
101.1 closed cup Ref 55,64,79
99.0 closed cup Ref 42

Autoignition Temp [C]

Dielectric Constant

9.41 @30C Ref Dean

Dipole Moment [debyes]

2.23 @20C Ref 80
2.53 @25C Ref Dean

Page 3 of 5

Entry Number 194

CHEMICAL AGENT SIMULANT DATA CENTER

METHYL SALICYLATE	Hygroscopicity
Critical Temp [C]	O/W Partition Coefficient [LogP] 2.46 Ref 72 2.55 Ref 72 (selected)
Critical Pressure [atm]	Solubility Parameter [H] 18.6 Ref 79
Critical Volume [cc/mole]	Toxicity LD50,oral,rat-0.887gm/kg Ref 55 LD50,oral,rabbit=2.8gm/kg Ref 55 LD50,oral,dog=2.1gm/kg Ref 55 inh,rat,2H 7hr exps of 700mg/m3-no effect Ref 64 avg LD human child=10ml Ref 42,64 avg LD human adult-30ml Ref 42,64 acceptable daily intake-500micrograms/kg Ref 64
Critical Density [gm/cc]	
Water Solubility slight	Solubility Value [gm/ml] 0.87 030C Ref 42,79
Hydrolyses Rate	
Industrial Application used as flavorant used in perfumes used as analgesic	
Page 4 of 5	Entry Number 194

CHEMICAL AGENT SIMULANT DATA CENTER

Chemical Reactivity

Simulant Application

used in numerous applications as an HD simulant.
used as an intake simulant in training exercises.

Comments

contact angle data on various surfaces available. Ref 79

Page 5 of 5	Entry Number 194	METHYL SALICYLATE

* * * * * * * * *

Chemical Name: Methyl salicylate
CAS Registry Number: 119-36-8
RTECS: VO4725000
Formula: C6H4(OH)(COOCH3)

SYNONYMS:

2-Hydroxybenzoic acid methyl ester
Betula oil
Methyl 2-hydroxybenzoate
Methyl salicylate
Oil of wintergreen
Sweet birch

Press <return> to continue, "q" to quit.

Teaberry oil

Property	Value		Condition		References
Boiling point	223.300	^C			11
Flash point	101.100	^C			11
Melting point	-8.625	^C			52
Molecular weight	152.140				52
Octanol/H2O part. coef.	275.400				59
Refractive index	1.536		20.000	^C	63
Soil sorption part. coef.	107.200				59
Solubility (water)	0.086	g/100 ml	20.000	^C	63
Specific gravity	1.184		25.000	^C	52
Vapor pressure	1.000	mm Hg	54.000	^C	11
Vapor specific gravity	5.240				11
Volatility	757.000	mg/m3	25.000	^C	63

DESCRIPTORS:

Methyl salicylate belongs to a class of compounds known as

Press <return> to continue, "q" to quit.

organic esters.

CHEMICAL AND PHYSICAL PROPERTIES:

Methyl salicylate is a colorless, to pale yellow oily liquid with the characteristic odor and taste of wintergreen. The compound is slightly soluble in water and highly soluble in chloroform, ether, alcohols, and glacial acetic acid.(52)

MILITARY APPLICATION:

Using human volunteers and a simulant consisting of Tinopal SWN and methyl salicylate thickened with poly methyl methacrylate,(1) the Army uses methyl salicylate to perform entry/exit tests for collective protection, NBC shelters.

INDUSTRIAL APPLICATION:

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Methyl salicylate is used in the perfume and flavoring industries and medicinally as a counterirritant in some ointments or linaments.(11)

ENVIRONMENTAL LAWS AND REGULATIONS:

Methyl salicylate is listed in the TSCA inventory.(45) DOT does not list it as a hazardous material, the RCRA does not list it as a hazardous waste, and the CERCLA and the FWPCA do not list it as a hazardous substance.

TOXICOLOGY:

Mutagenicity; No information found.
Reproductive Effects; Methyl salicylate caused reproductive effects in the offpsring of rats that were administered oral doses at a TDLo value of 36,540 mg/kg.(45)
Tumorigenicity; When injected intraperitoneally into mice 8 weeks

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old, methyl salicylate produced lung and thorax tumors(45) at doses at a TDLO value of 2400 mg/kg.

Ecotoxicity; Methyl salicylate is a phenolic ester that occurs naturally in a number of plants, including Gaultheria procumbens L., Betula lenta L. (sweet birch), Burnum dilatatum, and Betula alba L. (European white birch).(52)

Human Exposure Criteria: Currently, no TLV-TWA value has been established for methyl salicylate. However, it may cause severe poisoning and death when ingested in relatively small amounts (average lethal dose; 10 ml in children, 30 ml in adults).(52) The FDA lists methyl salicylate as a safe, indirect, food additive and adhesive when used in accordance with 21 CFR 175.105. The Army Surgeon General's Office has approved methyl salicylate containing tinopal SWN thickened with poly methyl methacrylate for entry/exit tests of the collective protection, NBC shelters when human volunteers are used.(1)

Route	Species	Dose	Toxic Effects (Reference)

Press <return> to continue, "q" to quit.

Oral	Human	506 mg/kg	LDLo (45)
	Rat	887 mg/kg	LD50 (45)
	Dog	2100 mg/kg	LD50 (45)
	Rabbit	1300 mg/kg	LD50 (45)
	Guinea pig	1060 mg/kg	LD50 (45)
Skin	Rabbit	500 mg/24 hr.	Moderate Irritation (45)
	Guinea pig	500 mg open	Severe Irritation (45)
Eye	Rabbit	500 mg/24 hr.	Severe Irritation (45)
	Guinea pig	500 mg open	Severe Irritation (45)

CHEMICAL REACTIVITY:

Alkali and Alkaline Earth Metals; The hydrogen on the phenoxy oxygen atom can be readily removed to produce hydrogen gas and heat. Hydrogen gas generates explosive mixtures with air.

Azo Compounds; The aromatic and aliphatic diazo compounds react exothermally with phenols to form thers and nitrogen gas.

Press <return> to continue, "q" to quit.

Caustics; Methyl salicylate is converted to the corresponding salicylic acid salt and methyl alcohol with the generation of heat. Methyl alcohol is flammable and toxic.

Epoxides; The phenolic compounds may rupture the epoxy carbon-oxygen bond to cause polymerization.

Isocyanates; The phenols can combine with the isocyanates to produce carbamic esters and heat.

Mineral Acids; In excess, mineral acids react with methyl salicylate to cause hydrolysis and decomposition of the ester; heat is generated.

Nitrides; The ionic nitrides react with aromatic hydroxy compounds to produce a flammable gas and heat.

Organic Peroxides; The organic peroxides may oxidize the phenolic group of methyl salicylate to produce a quinone; some heat may evolve.

Oxidizing Mineral Acids; Exhaustive oxidation of methyl salicylate by oxidizing mineral acids causes its decomposition, heat generation, and possible ignition of the ester. Depending on conditions, salicylic acid may be produced and subsequently decarboxylate. Methyl alcohol, another product, is toxic and

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flammable. Phenolic compounds are readily oxidized.

Strong Oxidizing Agents; Oxidation of methyl salicylate by strong oxidizers can generate a tremendous amount of heat. Reaction products include ketones, carboxylic acids, and carbon dioxide.

Strong Reducing Agents; The strong reducing agents may remove the phenoxy hydrogen. Hydrogen gas and a tremendous amount of heat are produced. The hydrogen gas forms explosive mixtures with air.

Water Reactives; Because the water reactive materials can be very active with methyl salicylate, it should not be mixed with them.

ENVIRONMENTAL FATE:

ENVIRONMENTAL FATE/EXPOSURE SUMMARY - ENVS
Methyl salicylate is produced in significant quantities and is used in perfumes and sunburn lotions and in foods, beverages and pharmaceuticals. It is not known how much methyl salicylate is

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released to the environment. In soil, methyl salicylate is likely to hydrolyze or biodegrade and will leach to groundwater. It is not expected to volatilize significantly from soil. In water, methyl salicylate should hydrolyze at alkaline pH and may biodegrade, but will neither evaporate readily nor adsorb appreciably to sediments. Methyl salicylate is not likely to bioconcentrate in aquatic organisms. No atmospheric fate data for methyl salicylate was available, but the ester is expected to be oxidized with an estimated half-life of 5.7 days by hydroxyl radicals.

NATURAL OCCURRING SOURCES - NATS

Methyl salicylate occurs in the leaves of Gaultheria procumbens L. Ericaceae, in the bark of Betula lenta L. Betulaceae(52) and in the leaves of Burnum dilitatum(11).

ARTIFICIAL SOURCES-ARTS

Methyl salicylate is used as a flavoring in foods, beverages, pharmaceuticals(26) and dentifrices(173), as a fragrance agent in cosmetics and perfumes (173) , as a UV-absorber in sunburn lotions(26), and as a counter-irritant in some ointments and liniments (11). Methyl salicylate is also used as a carrier for

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fabric dyes and as a UV stabilizer in acrylic resins (173). The military uses methyl salicylate in combination with Tinopal SWN and thickened with polymethyl methacrylate to perform entry/exit tests for collective protection, NBC shelters(118).
TERRESTIAL FATE: Methyl salicylate will hydrolyze in moist alkaline soils. Although no half-life can be estimated for the soil matrix, the hydrolosis should be at least as fast as in water. Biodegradation may also be an important process in soils. Methyl salicylate is not expected to bind tightly to soils and should, therefore, eventually leach to groundwater unless the compound completely hydrolyzes first.
AQUATIC FATE: Methyl salicylate is expected to hydrolyze in water at pH 7.5 with an estimated half-life of 22 days (estimated from data in ref. 174 and 175). Generally speaking, the more basic the conditions, the faster will be the hydrolysis rate. Methyl salicylate may photolyze under environmental conditions. Due to the low vapor pressure and moderate solubility of methyl salicylate, little or no volatilization of the ester from wate2 is expected.
ATMOSPHERIC FATE: Information concerning the fate of methyl

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salicylate in the atmosphere was not available. According to Graedel(124), the atmospheric chemistry of esters is expected to resemble that of alkanes except that esters will react more rapidly with hydroxyl radicals than will the corresponding alkane. The increased rapidity of hydrogen abstraction is the result of the decreased strength of the C-H bonds in the esters compared to that of the alkanes. Methyl salicylate, if it enters the atmosphere, is thus expected to degrade ultimately to small, oxygenated organic molecules. A half-life of 5.71 days was estimated for the reaction of methyl salicylate with hydroxyl radicals(171).

BIODEGRADATION-BIOD

Methyl salicylate in a five day BOD test exhibited a value of 55-57% of the theoretical BOD(176). Significant biodegradation of methyl salicylate in the environment would be expected from this result; however, no data concerning biodegradation in natural waters or soil could be located.

ABIOTIC DEGRADATION-ABIO

Magid and Larsen(174) determined a rate constant of 1.59 X 10-5 sec-1 for the hydrolysis of methyl salicylate at pH 9.2 and a

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temperature of 25^C.. A half-life value of 12.1 hours was calculated from this rate constant . Senent et al (175) determined an hydrolysis rate constant of 3.62 X 10-3 min-1 at a temperature of 24^C and pH 11.26. A half-life value of 3.2 hours was calculated from this rate constant. Data from both these studies indicate a general increase in rate constant with increasaing pH. Although the two first order rate constants do not lead to identical second order rate constants , an approximate half-life at pH 7.5 of 22 days can estimated. The absorption maximum of a methanol solution of methyl salicylate is 305 nm(177).

One photolysis study was performed which yielded a half-life of methyl salicylate in solution of about 48 min (178). The exact medium was not identified, but the authors stated that compounds with low water solubilities were dissolved in a 10% ethanol-water mixture. Based on the concentration of methyl salicylate which was used (0.35g/100ml), and the water solubility of the ester of 0.086g/100ml, it is likely that the result above was obtained using an ethanol-water mixture or absolute ethanol. The UV dose used in the study was 0.0077 erg/cm2/min, and the UV wavelengths ranged

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from 300 nm to 400 nm with a maximum at 350 nm. Direct photolysis may, therefore, be an important degradative process in the environment; no available data, however, were collected under environmental conditions.

BIOCONCENTRATION-BIOC

The estimated octanol/water partition coefficient of methyl salicylate suggests that the ester will not bioconcentrate in fish.

SOIL ADSORPTION/MOBILITY-KOC

The low estimated soil sorption partition coefficient of methyl salicylate suggest that the ester will not adsorb to soils or sediments. It is expected, therefore, that methyl salicylate will leach extensively and eventually reach the groundwater provided complete hydrolysis does not occur first.

VOLATILIZATION FROM WATER/SOIL-VWS

The low vapor pressure and moderate water solubility of methyl salicylate and its ability to hydrogen bond suggest that the ester will not volatilize appreciably from water or soils.

FOOD SURVEY VALUES-FOOD

Furia and Bellanca (179) reported methyl salicylate concentrations of 54 ppm in bakery goods, 840 ppm in candy, 59 ppm in non-

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alcoholic beverages, 8400 ppm in chewing gum, 27 ppm in ice cream and 200 ppm in syrups.

PROBABLE ROUTES OF HUMAN EXPOSURES-RTEX

The primary route of human exposure is likely the consumption of consumer products which contain methyl salicylate as a flavoring agent. Methly salicylate is used in chewing gum, baked goods, syrups, candy, non-alcoholic beverages and ice cream. Other potential routes of exposure include the use of perfumes and sunburn lotions containing methyl salicylate.

References can be obtained by choosing option number five from the main menu.

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APPENDIX D

ESTIMATION OF THE SPREAD OF METHYL SALICYLATE

The volume of a liquid drop and the area which wets the surface determines the area spread upon and covered by the drop. (Long, Wallace[9]) This area eventually covered is directly porportional to the force of impact of the drop and its subsequent splatter or breakup. The radius (r) of the contact circle from the resultant drop can be estimated from the contact angle (Θ) using the following equation: r(cm)

$$\tan \Theta = \frac{4xV}{r^3} \times \frac{E + E^3/8 + E^5/192 + E^7/9216 + E^9/737280}{E + E^3/12 + E^5/384 + E^7/23040 + E^9/2211840} \qquad (1)$$

where:

V = Drop Volume (cm^3)

$$E = r \times \left| \frac{d \times g}{t} \right|^{1/2}$$

d = liquid density (g/cm^3)

g = acceleration of gravity = 980 cm/s^2

t = liquid surface (dynes/cm)

This equation is reported accurate to within 10% for values of Θ up to 30 degrees.

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APPENDIX E

MATERIAL SAFETY DATA SHEET FOR K125

Date MSDS Prepared: Date:
By: T. DERAM
Rev.: JAN. 1986

U.S. DEPARTMENT OF LABOR
Occupational Safety and Health Administration

Form Approved OMB No. 44-R1367

MATERIAL SAFETY DATA SHEET

Required under USDL Safety and Health Regulations for Ship Repairing, Shipbuilding, and Shipbreaking (29 CFR 1915, 1916, 1917)

SECTION I

Reseller

MANUFACTURER'S NAME	EMERGENCY TELEPHONE NO.
BUEHLER® LTD.	312/295-6500

ADDRESS (Number, Street, City, State, and ZIP Code)
41 Waukegan Road, Lake Bluff, IL 60044

CHEMICAL NAME AND SYNONYMS	TRADE NAME AND SYNONYMS
Methyl Methacrylate Polymer	#20-3552 PLASTIC POWDER
CHEMICAL FAMILY: Methyl Methacrylate Polymer-Acrylic	FORMULA

SECTION II - HAZARDOUS INGREDIENTS

PAINTS, PRESERVATIVES, & SOLVENTS	%	TLV (Units)	ALLOYS AND METALLIC COATINGS	%	TLV (Units)
PIGMENTS NONE			BASE METAL N/A		
CATALYST NONE			ALLOYS N/A		
VEHICLE NONE			METALLIC COATINGS N/A		
SOLVENTS NONE			FILLER METAL PLUS COATING OR CORE FLUX N/A		
ADDITIVES NONE			OTHERS N/A		
OTHERS NONE					

HAZARDOUS MIXTURES OF OTHER LIQUIDS, SOLIDS, OR GASES	%	TLV (Units)
NONE		

SECTION III - PHYSICAL DATA

BOILING POINT (°F.)	N/A	SPECIFIC GRAVITY (H_2O=1)	N/A
VAPOR PRESSURE (mm Hg.)	N/A	PERCENT, VOLATILE BY VOLUME (%)	N/A
VAPOR DENSITY (AIR=1)	N/A	EVAPORATION RATE (_____ =1)	N/A
SOLUBILITY IN WATER	N/A		
APPEARANCE AND ODOR	FREE FLOWING POWDER, NON-VOLATILE		

SECTION IV - FIRE AND EXPLOSION HAZARD DATA

FLASH POINT AND METHOD USED	FLAMMABLE LIMITS	LEL	UEL
TAG, OPEN CUP 300°F			

EXTINGUISHING MEDIA
POLYMER MUST BE HEATED ABOVE DECOMPOSITION TEMPERATURE TO RELEASE VAPORS
SPECIAL FIRE FIGHTING PROCEDURES THAT WILL BURN.

ABC DRY POWDER, CO_2 WATER

UNUSUAL FIRE AND EXPLOSION HAZARDS
ONLY HAZARDOUS UNDER DUSTY CONDITIONS, SUSPENDED IN AIR AND IGNITED.

- NONFLAMMABLE -

SECTION V - HEALTH HAZARD DATA

THRESHOLD LIMIT VALUE	N/A
EFFECTS OF OVEREXPOSURE	N/A

EMERGENCY AND FIRST AID PROCEDURES

NO UNUSUAL PROCEDURES REQUIRED. IF HANDLED IN A WAY THAT CREATES DUSTY CONDITIONS, OPERATOR SHOULD WEAR APPROVED DUST RESPIRATOR.

SECTION VI - REACTIVITY DATA

STABILITY	UNSTABLE		CONDITIONS TO AVOID
	STABLE	X	N/A

INCOMPATABILITY (Materials to avoid)

HAZARDOUS DECOMPOSITION PRODUCTS

HAZARDOUS POLYMERIZATION	MAY OCCUR		CONDITIONS TO AVOID
	WILL NOT OCCUR	X	N/A

SECTION VII - SPILL OR LEAK PROCEDURES

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED

SWEEP UP AND DISPOSE IN APPROVED LANDFILL - NON HAZARDOUS

WASTE DISPOSAL METHOD INCINERATION, LANDFILL

SECTION VIII - SPECIAL PROTECTION INFORMATION

RESPIRATORY PROTECTION (Specify type)

None required under normal use

VENTILATION	LOCAL EXHAUST	YES	SPECIAL
	MECHANICAL (General)		OTHER

PROTECTIVE GLOVES	NONE	EYE PROTECTION	RECOMMENDED

OTHER PROTECTIVE EQUIPMENT NONE

SECTION IX - SPECIAL PRECAUTIONS

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORING NONE

OTHER PRECAUTIONS NONE

The data and information as stated was furnished by the manufacturer and supplier of this product. BUEHLER, LTD. cannot warrant the accuracy of this information, and shall not be responsible or liable for any damage that may result, should any of the information be erroneous.